Remarks/Arguments

The foregoing amendments to the claims are of a formal nature and do not add new matter. Claims 119-138 are pending in this application and are rejected on various grounds. The rejections to the presently pending claims are respectfully traversed.

Priority

Applicants rely on the 'Mixed lymphocyte reaction' assay for patentable utility in this case. This utility was first disclosed in International Application PCT/US00/05841, filed March 2, 2000, priority for which has been claimed in this application. Further, the PRO1346 sequence and the nucleic acid encoding it was first disclosed in U.S. Provisional application 60/097661, filed 8/24/1998, (as SEQ ID NO: 2 and 1), priority for which has also been claimed in this application. Hence, the present application is at least entitled to an effective filing date of **March 2, 2000.**

Information Disclosure Statement

Applicants submit an IDS separately enlisting references recited in the Blast report in order to be compliant with 37 C.F.R. § 1.98(a)(1). Consideration of this Information Disclosure Statement is respectfully requested.

Specification

A. The disclosure was objected to by the Examiner as containing "embedded hyperlink and/or other form of browser-executable code." The foregoing amendment to the specification which deleted all embedded hyperlinks, is believed to overcome the present objections.

B. The title of the invention has been amended to better describe the claimed invention.

Accordingly, Applicants believe that all objections to the specification have been overcome and should be withdrawn.

Claim Objections

The syntax of claims 119-131 have been amended to remove references to Figures. Thus, Applicants believe this objection has been overcome and should be withdrawn.

Claim Rejections – 35 USC § 101 and 35 USC § 112, first paragraph-enablement

A. Claims 119-138 were rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by a specific, substantial and credible asserted utility or well established utility."

7A. Claims 119-138 are also rejected under 35 U.S.C. §112, first paragraph for failing to adequately teach how to use the instant invention. Applicants respectfully disagree with and traverse the rejection to the remaining claims.

Utility Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance with the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: **"If the (A)pplicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion**

would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the Applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

To overcome the presumption of truth based on an assertion of utility by the Applicant, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. **Absolute predictability is not a requirement.**

Only after the Examiner has made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence.

Further, the legal standard with respect to *in vitro* or animal model data providing pharmacological activity has been commented on in *Cross v. Iizuka*, 753 F.2nd 1040, 1051, 224 USPQ 739, 747-48 (Fed. Cir. 1985):

> "We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vitro* utility."

Furthermore, M.P.E.P. 2107.03 (III) states that:

> "If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process."

Thus, the legal standard accepts that *in vitro* or animal model data is acceptable utility as long as the data is "reasonably correlated" to the pharmacological utility described.

Arguments

PRO217 has utility

Without acquiescing to the propriety of this rejection, but solely in the interest of expediting prosecution in this case, Applicants submit a declaration with supportive references from the art to show that PRO217 has immunostimulant activity.

Applicants submit a declaration by Sherman Fong, Ph.D. of Genentech, Inc., an expert in the field of Immunology and co-inventor of the present application, to show that there are specific immune stimulant utilities for compounds identified by an MLR assay. The Declaration explains how the MLR reaction was performed in the instant application using peripheral blood mononuclear cells (PBMCs), which contain responder T-cells, and allogenic, pre-treated (irradiated) PBMCs, which predominantly contained dendritic cells. As Dr. Fong emphasizes, immunostimulants are important and are very desirable in the treatment of cancer and in enhancing the effectiveness of previously identified treatments for cancer. Supportive evidence also comes from teachings in the art like Steinman *et al.* (Exhibit B) who states that "...**medicine needs therapies that enhance immunity or resistance to infections and tumors**. (page 1, column 1, line 7; emphasis added)". Further teachings like Peterson *et al.* (Exhibit D) show that, recently, the immune stimulant IL-12, was successfully used in a cancer vaccine trial to treat melanoma. Further, as Dr. Fong explains regarding the IL-12 melanoma trial:

> "Due to the immune stimulatory effect of IL-12, **the treatment provided superior results** in comparison to earlier work, where the patients' own dendritic cells were prepared from peripheral blood mononuclear cells (PBMCs) treated with antigens, then cultured *in vitro* and returned to the patient to stimulate anti-cancer response" (Emphasis added).

Further, Dr. Fong's declaration clearly states that:

> "A PRO polypeptide shown to stimulate T-cell proliferation in the MLR assay of the present invention with an activity of at least 180% of the control is expected to have the type of activity exhibited by IL-12 and would find practical utility as an immune stimulant".

Accordingly, the positive results obtained in this assay clearly establish the stated utility for the

polypeptides claimed and accordingly, the nucleic acids encoding these polypeptides also have utility. The specification, in turn, enables one skilled in the art to use the compounds for the asserted purpose.

By the foregoing arguments and supportive evidence, Applicants have established that the MLR reaction is a generally recognized assay to assess the immunostimulatory activity. Thus, besides the previously asserted immunostimulatory uses of PRO 217 and its encoding nucleic acids, for example, in the treatment of viral infections like HIV or Epstein Barr viral infections, Applicants assert other utilities in the treatment of cancers like melanoma. Further, since the legal standard accepts *in vitro* as acceptable utility and the data is "reasonably correlated" to the pharmacological utility based on the discussions above, a valid case for utility has been made and would be considered credible by a person of ordinary skill in the art. For the same reason, one skilled in the art at the priority date of the present application would have reasonably accepted this utility for the PRO217 encoding nucleic acids.

Thus, Applicants believe they have established patentable utility for PRO1346 and its encoding nucleic acids claimed in the present application and this rejection should be withdrawn.

Claim Rejections – 35 USC § 112, first paragraph

B. Claims 119-138 are also rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and /or use the invention.

The Examiner pointed out that the deposit of biological material made under the Budapest Treaty for enablement of the current invention needs the current address of the ATCC and a declaration or statement stating that all restrictions imposed by the depositor on the public be irrevocably removed. Applicants submit that the ATCC address recited on page 563, line 10-11 is correct and further add requisite assurances into the specification to remove irrevocably all restrictions imposed by the depositor on the availability of deposited material to the public upon the granting of the pertinent U.S. patent. Accordingly, this rejection should be withdrawn.

C. Claims 119-138 are also rejected under 35 U.S.C. §112, first paragraph because, according to Examiner, "the specification, while being enabling for SEQ ID NO: 313 and 314,

does not reasonably provide enablement for polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity to SEQ ID NO:314, ATCC No 203128, its extracellular domain or fusion proteins. Applicants respectfully traverse this rejection.

As discussed above, PRO1346 has utility based on the MLR assay as an immunostimulator and its antagonists, as immunosuppressors. The claimed genus in the presently amended claims recite a functional recitation "wherein said polypeptide encoded by said nucleic acid is an immunostimulant" and hence the claimed molecules are defined by sequence as well as function. One skilled in the art would readily understand and appreciate, based on the general knowledge in the art and the disclosure of the present application, how to make and use the claimed invention at its effective filing date. Therefore, Applicants request reconsideration and withdrawal of this rejection.

Claim Rejections - 35 USC § 112, first paragraph- written description

Claims 119-138 are rejected under 35 U.S.C. 112, first paragraph because allegedly, the subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing.

Specific utility has been asserted in the present invention based on MLR activity of PRO1346 and the pending claims recite this functional feature for the nucleic acids encoding PRO1346 polypeptides. The pending claims are drawn to a genus of nucleic acids defined both by sequence and functional identity. It would have been obvious to one skilled in the art at the effective priority date, in view of Applicant's possession of the nucleic acid of SEQ ID NO:313 and the PRO1346 (SEQ ID NO:314), that the Applicant possessed these obvious variations and adaptations of SEQ ID NO:313 at the time of filing. Thus this rejection should be withdrawn.

Claim Rejections – 35 USC § 112, second paragraph

Claims 119-138 were rejected under 35 U.S.C. §112, second paragraph for being indefinite. The Examiner alleges that it was not clear whether or not the protein encoded by the polynucleotide of the present invention was a soluble protein nor was it disclosed as being

expressed on a cell surface. The recitation "extracellular domain" and "lacking its associated signal sequence" was also indefinite.

Applicants submit that at least on page 205, lines 30-34, the present protein (NL7 polypeptide) is disclosed as having a transmembrane domain tentatively identified as extending from about amino acid position 31 to 50 in the NL7 amino acid sequence (Figure 228, SEQ IN NO:314). Further, part (d) of the instant claims have been deleted for clarity. Accordingly, Applicants submit that the phrase "the extracellular domain" is definite and respectfully request that this rejection be withdrawn.

Claims 132-134 was rejected as vague and indefinite for reciting the term "hybridizes" and "stringent" without recitation of any conditions in each case.

Applicants have amended Claim 132 to recite the exact "stringent conditions" used during hybridization. Support for this amendment is found in the specification at least at page 312, line 33 to page 313, line 5. Accordingly, Applicants submit that the claims are definite and respectfully request that this rejection be withdrawn.

Claim Rejections - 35 USC § 102

Claims 119-138 are rejected under 35 U.S.C. §102(b) as being anticipated by Baker et al. (PCT/US99/12252, effective filing date 12/99).

As discussed under the section of priority, the PRO1346 sequence and its encoding nucleic acid was first disclosed in U.S. Provisional application 60/097661, **filed 8/24/1998**, (as SEQ ID NO: 2 and 1), priority for which has been claimed in the instant application. Further, the cited Baker publication is the PCT/US99/12252 application, to which priority has also been claimed in the instant application.

Therefore, Baker *et al.* is not prior art and Applicants request that this rejection be withdrawn.

Claims 132-134 are rejected under 35 U.S.C. §102(b) as being anticipated by Fernandez et al. (WO 00/061754, effective filing date 10/2000).

As discussed above, based on the effective priority date of **March 2, 2000** entitled to this application, Fernandez is not prior art. Thus, this rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C59). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: September 9, 2004

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